THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 52 (90/003,298)
Paper No. 50 (90/003,452)

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte MONSANTO COMPANY

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Appeal No. 1997-1547
Reexamination Nos. 90/003,298 and 90/003,452[1]

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HEARD: July 14, 1997

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Before WINTERS, WILLIAM F. SMITH, and GRON, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

[1] Merged Reexamination Proceeding for U.S. Patent No. 5,004,863, issued April 2, 1991, based on Application Serial No. 06/937,384, filed December 3, 1986.

DECISION ON APPEAL[2]

This is an appeal under 35 U.S.C. § 306 from the decision of the patent examiner that claims 13 through 15 of U.S. Patent 5,004,863 are not patentable. The patentability of claims 1 through 12 and 16 has been confirmed, and these claims are not the subject of this appeal.

Patented claims 1 and 13 through 15 read as follows:

1. A method of introducing genes into cotton plants and plant lines comprising the steps of:

exposing hypocotyl tissue of immature cotton plants to a culture of transformation competent non-oncogenic *Agrobacterium tumifaciens* harboring a Ti plasmid having a T-DNA region including both a foreign chimeric gene and a selection agent resistance gene, both genes including appropriate regulatory sequences so as to be expressed in the cells of cotton plants;

culturing the exposed tissue in the presence of a selection agent for which the resistance gene encodes for resistance so as to select for plant cells transformed with the T-DNA region;

inducing somatic embryo formation in the exposed tissue in culture; and

regenerating the somatic embryos into whole cotton plants.

13. Cotton plants produced by the method of claim 1 which include cells which comprise in their genome the foreign chimeric recombinant gene and the selection agent gene and which produce a foreign cellular product coded by the foreign gene.

14. Cotton somatic embryos produced by the method of claim 1.

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[2] This appeal is related to an appeal in the Merged Reexamination proceeding for U.S. Patent 5,159,135 (Reexamination Control Nos. 90/003,297 and 90/003,453; Appeal No. 1997-1546).

15. Cotton seeds produced by the plants of claim 3 [sic 13].

The references relied on by the examiner are:

Eur. Pat. App. 142,924 (Adang III) May 1985

Zhou et al. (Zhou 1983), "Introduction of Exogenous DNA into Cotton Embryos," Methods in Enzymology, Vol. 101, pp. 433-481, 1983.

Jian et al. (Jian), "A Molecular Demonstration of the Introduction into Cotton Embryos of exogenous DNA," Acta Biochimica et Biophysica Sinica, Vol. 16, No. 3, pp. 325-327, 1984.

Zhou (Zhou 1986), "Genetic manipulation of the Ovule After Pollination," Chapter 19 in Experimental Manipulation of Ovule Tissues, Chapman et al. (Eds.), Longman, New York, pp. 240-250, 1986.

The references discussed by the merits panel are:

Adang et al. (Adang I), "Insect Resistant Plants," Chemical Abstracts, Vol. 103, No. 9, Abstract No. 66080c, 1985.

Eur. Pat. App. 142,924 (Adang II), pages 1, 22 and 77 only. May 1985

The only rejection pending in this merged reexamination proceeding is that of claims 13 through 15 under 35 U.S.C. § 103 as unpatentable over Adang III taken with Zhou 1983 and either Jian or Zhou 1986. We reverse.

PRELIMINARY MATTERS

The provisions for reexamination of issued patents are set forth in 35 U.S.C. §§ 301-306. Section 303 provides in pertinent part:

> (a) Within three months following the filing of a request for reexamination under the provisions of section 302 of this title, the Commissioner will determine whether *a substantial new question of patentability* affecting any claim of the patent concerned is raised by the request . . . (emphasis added)

During the July 14, 1997 hearing of this appeal, patent owner Monsanto Company, citing In re Portola Packaging Inc., 110 F.3d 786, 42 USPQ2d 1295 (Fed. Cir. 1997), argued that the references now relied upon could not form the basis of a substantial new question of patentability because Adang, Zhou 1983 and Zhou 1986 had been previously considered by the examiner, and Jian was merely cumulative to Zhou 1986. Our first consideration, therefore, is whether the question of patentability at issue in this appeal is one previously considered and resolved.

In interpreting the statutory phrase "a substantial new question of patentability," the court in Portola Packaging noted that Congress, through the reexamination statute, authorized the PTO to reexamine an issued patent "within strictly defined limits." Specifically, "reexamination was only intended for those instances in which the examiner did not have all of the relevant prior art at his disposal when he originally considered the patentability of an invention." In re Portola Packaging Inc., 110 F.3d 786, 789-90, 42 USPQ2d 1295, 1298-99 (Fed. Cir. 1997). The court held that "a rejection made during

reexamination does not raise a substantial new question of patentability if it is supported only by prior art previously considered by the PTO in relation to the same or broader claims." Id. 110 F.3d at 791, 42 USPQ2d at 1300.

After considering patent owner's oral argument, we agreed that Portola Packaging was fairly implicated, and remanded this reexamination proceeding to the examiner to determine exactly which references or portions of references were relied on at each stage of prosecution of the '863 patent, to consider the issues raised by the decision in Portola Packaging, and to take appropriate action (Paper No. 46 in 90/003,298 and Paper No. 44 in 90/003,452). The examiner's position has not changed and we have before us now the examiner's Response to the Remand (Paper No. 48 in 90/003,298 and Paper No. 46 in 90/003,452) and patent owner's Comments on the Examiner's Response to the Remand (Paper No. 50 in 90/003,298 and Paper No. 48 in 90/003,452). We have taken the respective positions of the examiner and patent owner into account in reaching our decision.

We hold that the rejection before us is based, at least in part, on prior art not before the examiner during earlier prosecution, and so is based on a substantial new question of patentability. We set forth the following sequence of events in support of our conclusion:

Prosecution History

Serial No. 06/937,384

Application Serial No. 06/937,384 was filed on December 3, 1986. In the first action on the merits (Paper No. 6, February 3, 1988), claims 14 and 16 through 21 (equivalent to patented claims 13 and 15) were rejected under 35 U.S.C. § 102(b) as anticipated by a Chemical Abstracts publication, attributed to Adang (Adang I).[3] In responding to the rejection (Paper No. 7, August 15, 1988), applicant indicated that Adang I was based on European patent application 142,924, and supplied excerpts from the patent (Adang II). The Information Disclosure Statement (Form PTO-1449) which accompanied Paper No. 7 listed the patent without indicating which portions were supplied. By oversight or otherwise, the citation was not initialed by the examiner. Nevertheless, it appears from the record that only the title page (which included an abstract), and pages 22 and 77 of EP 142, 924 were before the examiner during the original examination procedure (page 7, Paper No. 7). A reference to Zhou et al.[4] was also submitted with applicant's response and discussed briefly (page 3, Paper No. 7); the citation of this reference on the Form PTO 1449 was initialed by the examiner.

Applicant made two arguments regarding Adang's work. First, that EP 142,924 (the document from which Adang I was generated) merely suggested the present invention

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[3] Adang et al., "Insect Resistant Plants," Chemical Abstracts, Vol. 103, No. 9, Abstract No. 66080c, 1985.

[4] Zhou et al. (Zhou 1983), "Introduction of Exogenous DNA into Cotton Embryos," Methods in Enzymology, Vol. 101, pp. 433-481 (1983).

and did not actually anticipate it; second, that neither Adang I nor Adang II was enabling. The rejection of the claims over the Chemical Abstracts publication was withdrawn in the examiner's next action without comment. Outstanding issues were ultimately resolved, and the application issued as Patent No. 5,004,863 ('863) on April 2, 1991.

Reexamination Request No. 90/002,721

The '863 patent was the subject of a previous reexamination proceeding, No. 90/002,721. In requesting reexamination (Paper No. 5, page 9), the third party requestor urged that claims 13 through 15 of the '863 patent were anticipated by Zhou 1983, the same reference cited during prosecution of the '863 patent. Requestor pointed out that patentee had stated upon citing the reference that "no biochemical data was presented in [Zhou 1983] to verify that transformation actually took place" and cited two additional references, including a 1986 reference to Zhou,[5] purporting to show that Zhou 1983 had indeed demonstrated successful transformation and thus anticipated the patented claims.

Reexamination was granted (Paper No. 5, June 12, 1992), however, the examiner subsequently confirmed that the claims of the '863 patent were patentable (Paper No. 7, October 8, 1992).

Merged Reexamination Requests 90/003,298 and 90/003,452

[5] Zhou (Zhou 1986), "Genetic Manipulation of the Ovule After Pollination," In: Experimental Manipulation of Ovule Tissues, Chapman, G.P. et al., Eds., Longman, New York, pp. 240-250 (1986).

There is only one rejection pending in this merged proceeding. According to the examiner claims 13 through 15 of the '863 patent are unpatentable over Adang taken with Zhou 1983 and either Zhou 1986 or Jian. In this proceeding, however, EP 142, 924 (Adang III) is relied on in its entirety. Jian is before the examiner for the first time.

The Three Adang References

Adang I. This is a commercial Chemical Abstracts publication and does not match the abstract on the title page of EP 142,924 (Adang II or Adang III), even though Chemical Abstracts identifies the European application as the source of the abstract. Adang I reads in pertinent part:

> The *Bacillus thuringienois* [sic *thuringiensis*] gene for the insecticidal crystal protein (*-endotoxin) is inserted into an *Agrobacterium tumifaciens* Ti plasmid . . . *Agrobacterium* contg. the recombinant Ti plasmid vector is then used to infect various whole plant and plant tissue . . . The crystal protein gene was then transferred via the Ti plasmid to cotton or tobacco cells in cultures and crystal protein-producing clones selected. Whole plants were regenerated from the selected clones by standard methods. These regenerated plants can be propagated by conventional means . . .

This affirmative disclosure of transformed cotton plants appears to be what the examiner relied on in rejecting original claims 14 and 16 through 21 under 35 U.S.C. § 102(b) during the prosecution of the '863 patent.

Adang II. In response to the rejection over Adang I, applicant supplied excerpts of European patent application 142,924 (Adang II); Adang II appears to consist of pages 1, 22 and 77 of EP 142,924. The abstract on page 1 differs considerably from the commercial abstract, Adang I. While it describes a method for introducing expressible

insecticidal protein structural genes into plant genomes by *Agrobacterium tumifaciens* Ti plasmid-mediated transformation, cotton is not mentioned at all. Page 22 suggests that the technique "in principle applies to any introduction of an insecticide structural gene into any plant species into which foreign DNA . . . can be introduced and in which said DNA can remain stably replicated" while page 77 lists cotton as one of the plants recommended for transformation.

Adang III. This is the entire text of EP 142,924 and was before the examiner for the first time in the present merged reexamination proceeding. The present rejection cites Adang III as the primary reference in a rejection under 35 U.S.C. § 103 and relies on that portion that discusses transformation by direct injection of DNA (e.g., page 33) to provide a nexus between Adang III and the secondary reference, Zhou 1983. Transformation by direct injection of DNA was not mentioned in either Adang I or Adang II, the only Adang references before the examiner in the original prosecution of the '863 patent.

Having considered these events, we have reached the conclusion that the subject matter of EP 142,924 (Adang III) relied in the rejection before us is not the same as that before the examiner in the original examination or in the first reexamination of the '863 patent. It follows that the present rejection does raise a substantial new question of patentability, and is properly before us for review.

THE EXAMINER'S REJECTION

Initially, we note that the patentability of process claims 1 through 12 and 16 of P.N. 5,004,863 has been confirmed, and is not at issue in this appeal. Product-by-process claims 13 through 15 depend from claim 1, and stand rejected under 35 U.S.C. § 103 as unpatentable over Adang III taken with Zhou 83 and either Zhou 86 or Jian.

Claim 13 is directed to genetically modified cotton plants produced by *Agrobacterium tumifaciens*-mediated transformation of hypocotyl tissue[6] from immature plants with a plasmid containing a T-DNA region which includes a "foreign chimeric gene" and a "selection agent resistance gene." Briefly, the hypocotyl tissue is infected with plasmid-carrying *Agrobacterium* and cultured on media containing the selection agent. Only cotton cells transformed by the plasmid, and expressing the selection agent resistance gene, will survive this step. Somatic embryogenesis[7] is induced in the surviving cultures, resulting in generation of modified whole cotton plants. Cotton plants meeting the limitations of claim 13 contain cells which include both the foreign and selection agent resistance genes in their genomes, and which also express the product encoded by the

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[6] That part of the axis of a plant embryo or seedling below the cotyledon (the first leaf or leaves developed by the embryo in seed plants).

[7] The process whereby an embryo with the potential to regenerate into a whole plant arises in tissue culture from non-gametic tissue (cotyledon, hypocotyl, etc.) rather than from a fertilized egg. See U.S. Patent No. 5,004,863; column 1, lines 48 *et seq.*

foreign gene. Claim 14 is directed to somatic cotton embryos produced by the process of claim 1. Finally, claim 15 is directed to cotton seeds produced by the plants of claim 13.

The examiner's rejection of the claims is premised on a combination of Adang III and Zhou 83. Zhou 86 and Jian were cited to reinforce the teachings of Zhou 83.

Adang III is principally directed to *Agrobacterium* Ti plasmid-mediated transformation of plants with genes encoding insecticidal structural proteins. The working examples demonstrate transformation of tobacco with a *Bacillus thuringiensis* gene encoding the insecticidal crystal protein, *-endotoxin (Bt toxin), and insertion of insecticidal genes into other plants, including cotton, is suggested. At page 33, the reference briefly mentions other vectors and methods of delivering them:

> Although the preferred embodiment of this invention incorporates a T-DNA-based Agrobacterium-mediated system for incorporation of the insecticide gene into the genome of the plant which is to be made insect resistant, other means for transferring and incorporating the gene are also included within the scope of this invention. Other means for the stable incorporation of the insecticide gene into a plant genome additionally include, but are not limited to, use of vectors based upon viral genomes, minichromosomes, transposons, and homologous or nonhomologous recombination into plant chromosomes. Alternate forms of delivery of these vectors into a plant cell additionally include, but are not limited to, direct uptake of nucleic acid, fusion with vector-containing liposomes, microinjection, and encapsidation in viral coat protein followed by an infection-like process.

In describing Adang III (at page 5 of the Answer), the examiner initially mentions "the insertion of foreign DNA encoding Bt toxin . . . , and a selectable marker gene" by *Agrobacterium* Ti plasmid-mediated transformation, but immediately shifts the focus of the

discussion to the portion of the reference quoted above, implicitly excluding *Agrobacterium* Ti plasmid-mediated transformation of plants from the rejection:

> Although Adang et al described Agrobacterial mediated transfer of T-DNA at length, other means of stably incorporating the foreign insecticidal gene were said to be known for delivering the vector to the plant cell and that these alternative means included direct DNA uptake and microinjection (page 33).

This shift in focus appears to be crucial to the rejection, because the examiner relies on the "other means of stably incorporating the foreign insecticidal gene" to establish a link to the secondary reference, Zhou 83.

Zhou 1983 discloses the results of attempts to produce transformed cotton plants by injecting donor cotton plant DNA into the axile placentae of flowering recipient cotton plants. Seeds ripened from the flowers were planted and offspring obtained, many of which resembled the donor plant in certain respects. Some of the plants grown from the seeds of the offspring maintained a resemblance to the donor plant.

According to the examiner's statement of the rejection:

> Adang et al provided the foreign DNA construction and the motivation to integrate that foreign DNA into the cotton genome by any available means; the secondary references provided an available means of how to put the foreign DNA into cotton. At the time this invention was made it would have been obvious to one of ordinary skill in the art to modify the primary reference with the teachings of the secondary references in order to insert the DNA encoding Bt toxin protein into cotton plants so as to make the cotton plants resistant to insect predation . . .

The proposed manner of combining the references leaves a great deal to conjecture. From the examiner's description of Adang III and nebulous statement of the rejection, we infer that the examiner concluded that it would have been obvious for one skilled in the art to transform cotton with Adang III's "foreign DNA construction" by an "alternative means," such as that taught by Zhou 83, as each reference either discusses or discloses transformation of cotton by direct injection of DNA.

We hesitate to comment on whether this would be an adequate basis for combining Adang III and Zhou 83 if both references mentioned direct injection in the same context or environment, but the fact is, they do not. Adang III suggests direct injection or microinjection of non-gametic cotton cells in tissue culture with foreign, heterologous DNA (bacterial genes encoding insecticidal proteins), while Zhou 83 discloses direct injection of fragmented DNA (from a donor cotton plant) into the egg cells and/or zygotes of a just-fertilized mature cotton plant.

Viewing each reference in its entirety, the link between the two is illusory. At best, the references describe parallel approaches to transforming cotton. Taking a step back, we cannot agree that the references lend themselves to the proposed combination and we see no reason, other than hindsight based on patent owner's disclosure, to modify Adang III to arrive at the claimed invention. In our judgment, the combined disclosures of the references are insufficient to reach the subject matter on appeal.

Moreover, in addition to a foreign gene (e.g., Adang III's insecticide gene), claims 13 through 15 require a "selection agent resistance gene" which provides for selection of transformed cells in tissue culture. The statement of the rejection does not specify what is included in the "foreign DNA construction," but the portion of Adang III relied on in the rejection concerns "stable incorporation of the insecticide gene." Even if that portion of Adang III mentioned a selection resistance gene, it would have no purpose or function in Zhou 83's method, as Zhou 83 teaches "regeneration of a plant through exogenous DNA directly introduced into the embryos of a living plant" and breeding "disease-resistant plant[s] by growing the [zero generation] seeds directly in a field, or select[ing] resistances to environmental factors by growing the seeds under specified conditions." See the paragraph bridging pages 441 and 442 of Zhou 83. The examiner has proposed no reason why one skilled in the art would incorporate the required "selection agent resistance gene" in a "foreign DNA construction" to be introduced into cotton by a process that deliberately avoids selection in tissue culture.

Finally, the cotton somatic embryo of claim 14 is wholly unaccounted for in the statement of the rejection. Somatic embryogenesis does not occur in the process outlined by Zhou 83, as whole plants are grown directly from fertilized and ripened seeds, rather than from non-gametic tissue.

35 U.S.C. § 103 requires that obviousness be determined on the basis of the claimed "subject matter as a whole." Where, as here, the determination of obviousness is

based on less than the entire claimed subject matter, the examiner's conclusion of unobviousness is unsound and cannot be maintained.

Accordingly, the rejection of claims 13 through 15 under 35 U.S.C. § 103 is reversed and the patentability of the claims is confirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

Sherman D. Winters Administrative Patent Judge	)
William F. Smith Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Teddy S. Gron Administrative Patent Judge	)

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